European Code against Cancer 4th Edition

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European Code against Cancer 4th Edition: Physical activity and cancer☆

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ABSTRACT

Physical activity is a complex, multidimensional behavior, the precise measurement of which is challenging in free-living individuals. Nonetheless, representative survey data show that 35% of the European adult population is physically inactive. Inadequate levels of physical activity are disconcerting given substantial epidemiologic evidence showing that physical activity is associated with decreased risks of colon, endometrial, and breast cancers. For example, insufficient physical activity levels are thought to cause 9% of breast cancer cases and 10% of colon cancer cases in Europe. By comparison, the evidence for a beneficial effect of physical activity is less consistent for cancers of the lung, pancreas, ovary, prostate, kidney, and stomach. The biologic pathways underlying the association between physical activity and cancer risk are incompletely defined, but potential etiologic pathways include insulin resistance, growth factors, adipocytokines, steroid hormones, and immune function. In recent years, sedentary behavior has emerged as a potential independent determinant of cancer risk. In cancer survivors, physical activity has shown positive effects on body composition, physical fitness, quality of life, anxiety, and self-esteem. Physical activity may also carry benefits regarding cancer survival, but more evidence linking increased physical activity to prolonged cancer survival is needed. Future studies using new technologies – such as accelerometers and e-tools – will contribute to improved assessments of physical activity. Such advancements in physical activity measurement will help clarify the relationship between physical activity and cancer risk and survival. Taking the overall existing evidence into account, the fourth edition of the European Code against Cancer recommends that people be physically active in everyday life and limit the time spent sitting.

Abbreviations: AICR, American Institute for Cancer Research; BMI, body mass index; CUP, continuous update panel; EU, European Union; GIS, geographic information system; GPS, geographic positioning system; IARC, International Agency for Research on Cancer; MET, metabolic equivalent of task; PAQ, physical activity questionnaire; RR, relative risk; SHBG, sex-hormone binding globulin; WCRF, World Cancer Research Fund; WHO, World Health Organization.

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1. Introduction

1.1. Physical activity and sedentary behavior by age group and gender, and trends over time

Enhanced industrialization and emerging technologies combined with less physically demanding occupations have resulted in people becoming more sedentary in their daily routines. Based on the World Health Organization's (WHO's) data of self-reported physical activity levels, 31% of adults worldwide and 35% of adults in Europe are physically inactive. Based on survey data from the European Union, there is considerable variation in levels of physical activity between countries. For example, less than 20% of the population in Italy, Austria, and Greece regularly engage in physical activity outside organized sport, whereas over 40% of the population is regularly physically active in Latvia, Denmark, and The Netherlands (Fig. 1). On average, across European countries men are more physically active than women. In addition, physical activity decreases with age in both men and women, with the most pronounced drop at ages 60 years or older [1].

A decline in adult physical activity levels has been accompanied by an increase in sedentary time, which has been attributed to enhanced television watching and computer use. According to a recent study of 20 countries worldwide, the median sitting time among adults is 300 min per day, and adults aged 18–39 years sit on average 60 min more per day than adults aged 40–65 years [2].

Compared with adults, physical activity patterns among children are sporadic, and extended periods of moderate or vigorous physical activity are infrequent. Current data from 105 countries worldwide show that 80% of 13–15-year-olds do not achieve 60 min of physical activity per day [1]. As illustrated by data from 30 European countries, physical activity levels show a decline through teenage years, and girls tend to be less physically active than boys (Fig. 2).

1.1.1. Trends in physical activity

Based on questionnaire data, studies from Spain, Sweden, England, and Finland show that adults' recreational physical activity has increased in the past 20–30 years [3–6]. In parallel, levels of occupational physical activity have fallen. For example, 30-year time trends in physical activity from 1972 to 2002 in Finnish adults show that the prevalence of recreational physical activity increased from 49% to 67% in women and from 66% to 77% in men, while the prevalence of occupational physical activity decreased from 47% to 25% in women and from 60% to 38% in men. Also, transportation physical activity decreased from 34% to 22% in women and from 30% to 10% in men [4].

Information on trends in physical activity in young people is sparse, and the limited data appear to be somewhat controversial. For example, decreases in physical activity have been reported for Czech boys aged 14–18 years between 1998 and 2000, and between 2008 and 2010 [7]. In contrast, the number of steps per day increased between 2000 and 2006 in Swedish boys and girls aged 7–9 years [8].

1.2. Definition of physical activity and sedentary behavior

Physical activity is considered to be any movement of the body that is brought about by the contraction of skeletal muscle that increases energy expenditure above the basal level. By comparison, *physical exercise* or exercise training is defined as a sub-component of physical activity that is planned, structured, and repetitive, and is aimed at improving or maintaining physical fitness [9]. Physical exercise is considered isometric or static if there is no movement of the limb, and isotonic or dynamic if there is movement of the limb. Depending on the intensity of exercise performed, physical exercise is considered aerobic if oxygen is available for muscle contraction and anaerobic if oxygen is unavailable. Aerobic exercise leads to increases in heart rate and energy expenditure,

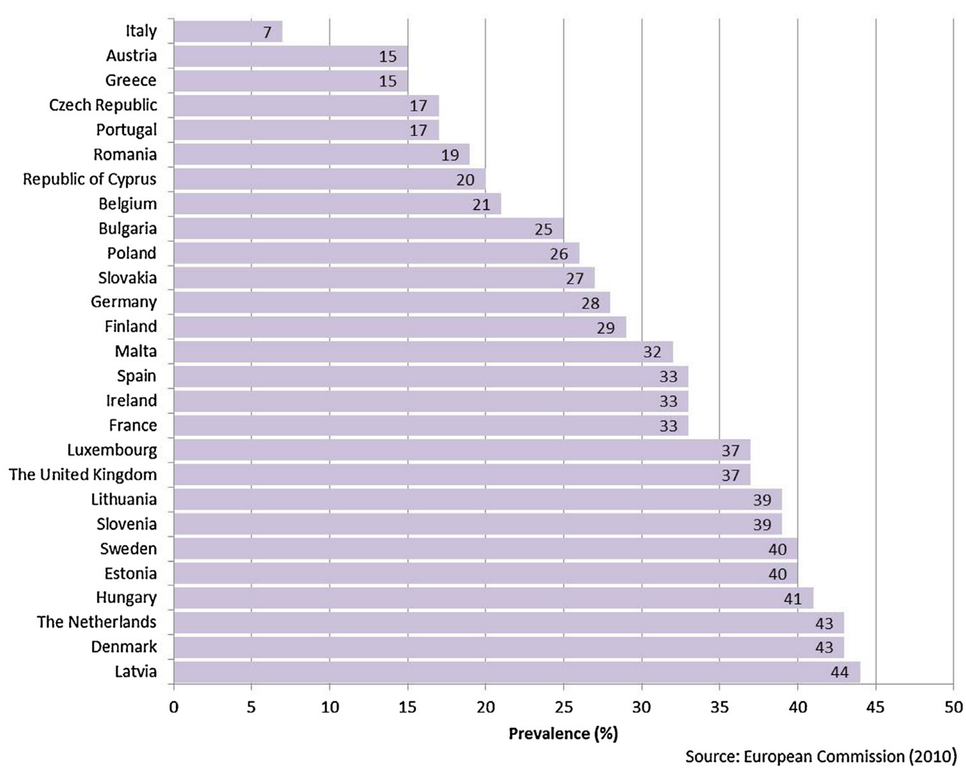

Fig. 1. Prevalence of regularly engaging in physical activity five times a week or more outside organized sport for 27 countries of the European Union [87]. Activities include cycling or walking from one place to another, dancing, and gardening. Data are based on the Eurobarometer survey commissioned by the European Commission's Directorate General for Education and Culture. The survey was conducted in October 2009 and involved 26,788 European citizens in 27 countries.

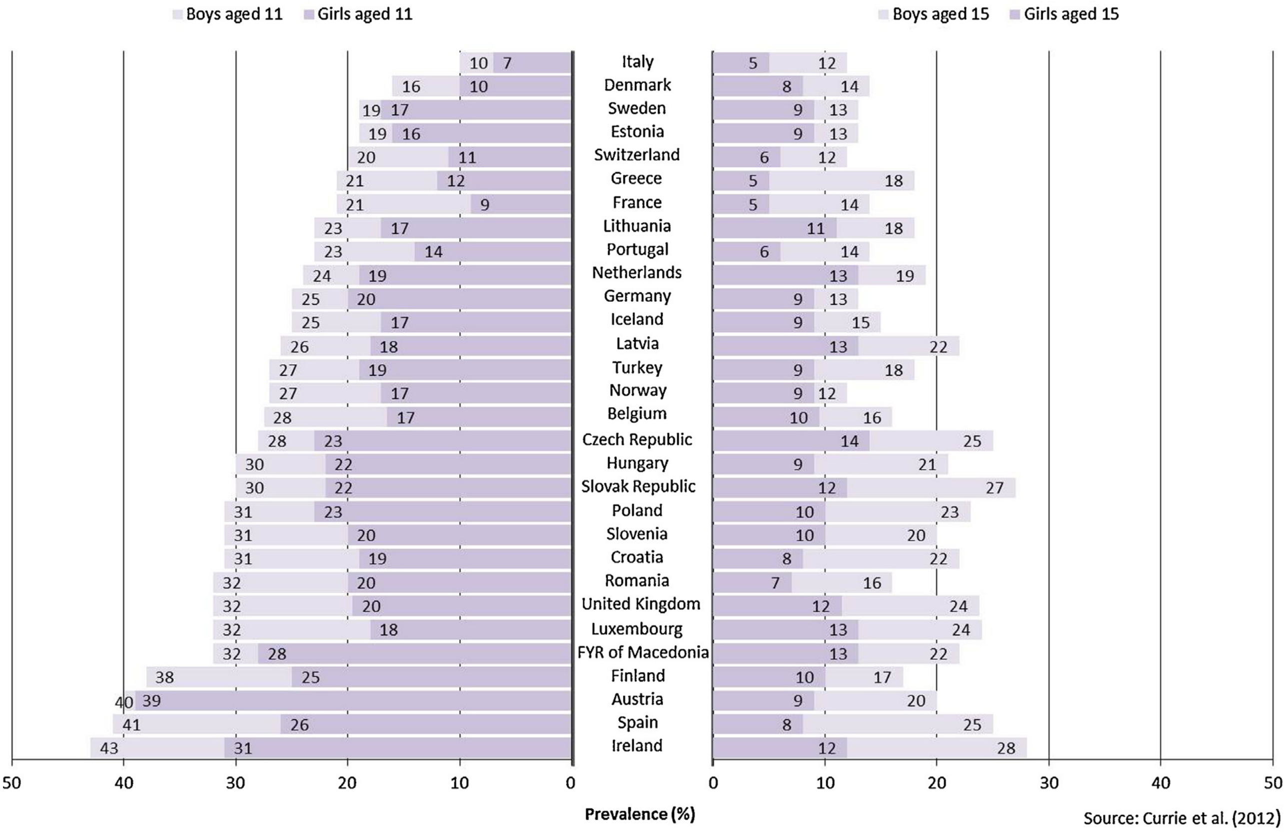

Fig. 2. Prevalence of daily moderate to vigorous physical activity among 11- and 15-year-olds in 30 European countries [88].

and includes walking, jogging, cycling, rowing, or swimming. Anaerobic exercise is performed to increase muscle size and strength, and typically involves activities such as resistance training or weight lifting.

Physical fitness differs from physical activity in that it describes a physiologic construct representing the ability to achieve a certain standard of physical performance [10]. The main determinants of physical fitness are age, sex, genetic factors, and habitual physical activity. Physical fitness generally shows stronger associations with health outcomes than physical activity, which may be partly explained by the imprecision in assessing physical activity relative to the ability to measure physical fitness [11]. Physical fitness can be classified into performance-related fitness and health-related fitness. Performance-related fitness includes attributes such as power, balance, and reaction time, whereas health-related fitness refers to cardiorespiratory fitness, body composition, muscular fitness, and flexibility.

Sedentary behavior has recently emerged as an independent health risk factor and it refers to activities with a low level of energy expenditure, such as sitting, lying down, or watching television or videos [12]. In Western populations, time spent in sedentary behavior is considerable, and it displaces time spent in physical activity, particularly light-intensity activity, thereby contributing to decreased total energy expenditure resulting from physical activity. The correlation between sedentary behavior and moderate to vigorous physical activity is minimal, and the time spent in sedentary behaviors has correlations that are distinct from those related to physical activity [13]. Laboratory and epidemiologic studies indicate that sedentary behavior has adverse deleterious metabolic and cardiovascular consequences that are independent of those observed with inadequate physical activity levels. For example, increased time spent viewing television is associated with enhanced waist circumference, systolic blood pressure, and plasma glucose levels – even among physically active individuals [14].

1.2.1. Components of physical activity

The dose or volume of physical activity is characterized by three components: namely the frequency and duration of the activity and the intensity with which the activity is carried out (Fig. 3). Frequency relates to the number of activity events during a specified time period, duration refers to the amount of time spent engaged in an activity event, and intensity describes the level of effort needed to perform a specific activity. The absolute intensity of physical activity is defined as the rate of energy expenditure. It is typically expressed as the metabolic equivalent of task (MET). One MET is defined as the energy expended sitting quietly, which is equivalent to an oxygen uptake of 3.5 ml per kg body weight per minute for an adult of 70 kg [15]. Activities are conventionally categorized into light-intensity activities (1.6–2.9 METs), moderate-intensity activities (3.0–5.9 METs), and vigorous-intensity activities ($\geq$6 METs). Relative intensity is expressed as the percentage of maximum oxygen uptake, maximum heart rate, or perception of exertion during exercise [16].

1.2.2. Types of physical activity

The main types of physical activity refer to specific domains, including occupational, household, transportation, and recreational (Fig. 4). Occupational activity is defined as any activity that is work-related and is performed within the time frame of an approximately eight hour work day. Examples of occupational activity include walking, lifting, hauling, pushing, shoveling, and packing boxes. Household activity covers activities, duties, and chores performed in the household, including yard work and child care. Transportation activity refers to activities that are performed for the purposes of going somewhere, such as walking or bicycling.

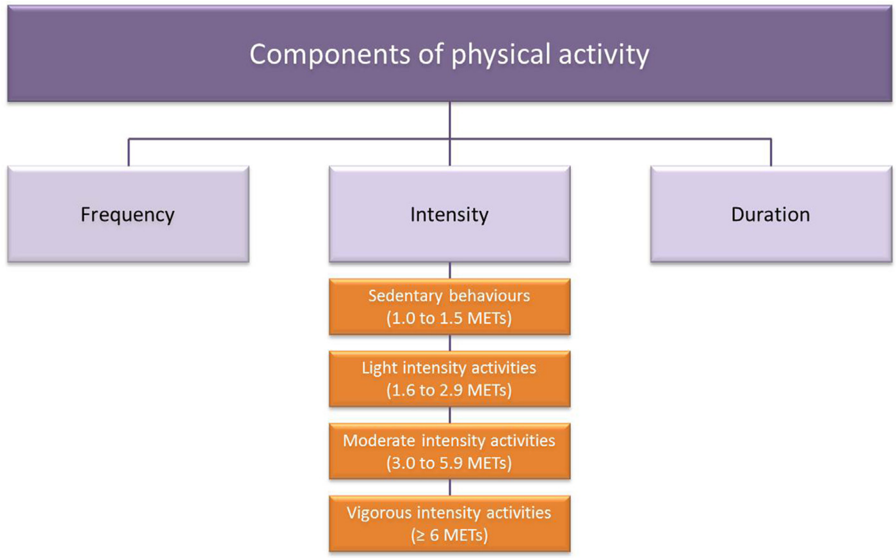

Fig. 3. Components of physical activity: the frequency and duration of the activity and the intensity with which the activity is carried out.

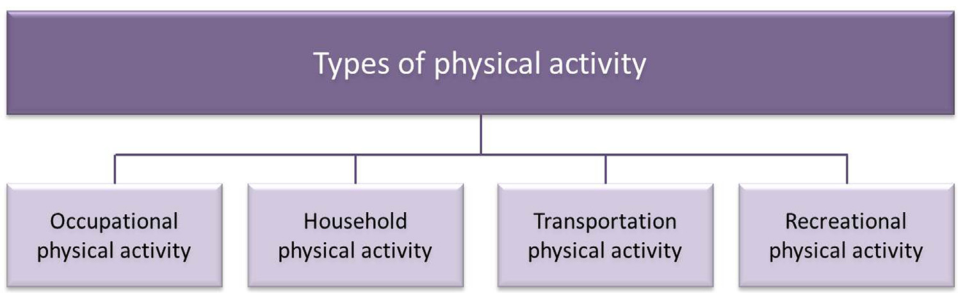

Fig. 4. Types of physical activity; the main types include occupational, household, transportation, and recreational activities.

Recreational activity includes activities that are undertaken during leisure time, such as walking, hiking, jogging, bicycling, swimming, tennis, or rowing.

1.3. Measurement of physical activity

Physical activity is a multifaceted process that is challenging to validly assess in free-living individuals. Numerous methods for measuring physical activity exist, each of which is characterized by specific strengths and limitations. Physical activity can be measured using two main types of methods: subjective methods and objective methods (Fig. 5). Subjective methods represent the most convenient, inexpensive, and practical ways to assess physical activity in the population on a large-scale level. Methods include physical activity questionnaires (PAQs), recalls, diaries, and logs. They can be self-administered or interview-based, and typically query physical activity during the past day, week, month, year, or lifetime. The main disadvantage of subjective methods is that they are subject to problems with recall or reporting that limit their validity. Measurement error in physical activity assessment may lead to underestimation or overestimation of the true effect of physical activity on cancer. Misclassification of physical activity levels can be minimized by using objective methods for physical activity assessment – such as pedometers or accelerometers, direct observation, and physiological measurements – which avoid the limitations of recall and reporting of physical activity. New technologies – such as computers, mobile phones, smart phones, geographic positioning system/geographic information system (GPS/GIS) technology, and speech recognition – are increasingly used to assess physical activity under free-living conditions. These novel technologies enable the collection of data on a large scale and will contribute to improved assessments of physical activity. However, objective measures of physical activity have some limitations, including financial costs, the potential for monitor displacement during long periods of data collection, and inaccurate assessment of certain activities such as upper body movements, incline walking, and water-based activities.

1.4. Relationship between the built environment and physical activity and sedentary behavior

Many studies have documented a relationship between walking and the characteristics of the built environment. Certain variables – such as proximity to potential destinations, and the presence of green spaces and bike paths – have been most consistently related to recreational walking [17]. Positive associations between perceived environmental dimensions and physical activity participation have been found in studies conducted in Belgium [18], Portugal [19] and France [20]. For European adolescents, heavy traffic is strongly inversely related to physical activity, whilst a secure bicycling or walking route from home to school is positively related to physical activity. In addition, outdoor fields and gymnasiums near home are positively related to physical fitness [21].

1.5. Necessity of examining the effects of physical activity independently of those related to adiposity

Because body mass is related to both physical activity and to cancer risk, it is important to distinguish the effects of physical

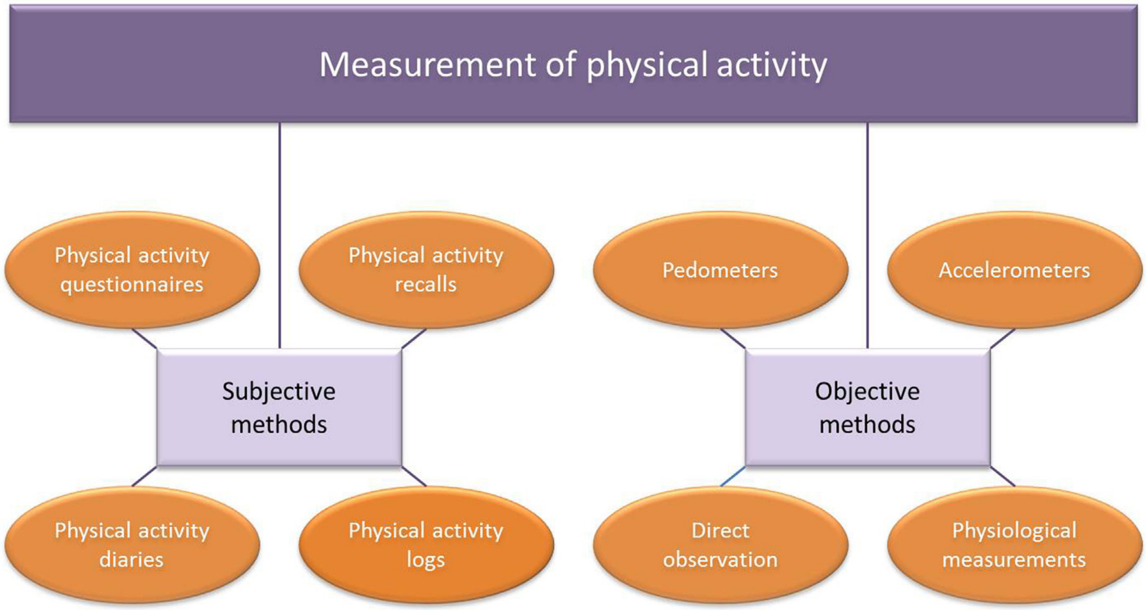

Fig. 5. Measurement of physical activity. This can be done using subjective methods and objective methods.

activity from those related to weight control. In addition, prevention of adiposity may mediate the relationship between physical activity and cancer, and controlling for adiposity could lead to underestimation of the overall effect of physical activity on cancer risk.

2. Physical activity and cancer

Insofar as physical activity is understood to be a factor that contributes to prevention of weight gain, physical activity may contribute to the prevention of diseases or conditions associated with being overweight or obese. Whilst there is a substantial evidence base for a beneficial effect of physical activity on cardiovascular health [22–25], evidence for the link with cancer is less well developed [26].

2.1. Cancer types related to inadequate physical activity

Physical activity can reduce the risk of developing some cancers (Table 1), partially independently of effects on body weight. Individual studies have suggested that physical activity might be protective against cancers of the lung, pancreas, ovary, prostate, kidney, and stomach, but evidence is modest in amount and is not consistent. On the other hand, the evidence that physical activity can protect against colon, breast and endometrial cancers is stronger.

Table 1
Estimated associations between high versus low physical activity levels and incidence of specific cancers.

Cancer type	Number of studies	Relative risk	Reference
Substantial evidence			
Colon	21	0.74 (0.68–0.80)	[29]
Endometrial	20	0.82 (0.75–0.90)	[89]
Breast	31	0.88 (0.85–0.91)	[75]
Weak or moderate evidence			
Prostate	24	0.94 (0.91–0.98)	[53]
Stomach	18	0.90 (0.76–1.06)	[90]
Ovary	9	0.89 (0.79–1.01)	[91]
Kidney	19	0.89 (0.80–0.99)	[54]
Lung	14	0.77 (0.73–0.81)	[92]
Pancreas	5	0.72 (0.52–0.99)	[52]

As discussed earlier (Section 1.3), quite apart from the sparse data available for some cancers, the lack of consistency in the methods used to quantify physical activity has proved a limitation to data analysis, and this has sometimes precluded dose–response meta-analyses for some cancers. Further, the difficulty in accurately assessing physical activity and the variability in the definitions of low and high levels of physical activity have led to quite large differences in risk estimates between studies.

2.1.1. Colon cancer

There is substantial evidence linking physical activity with reduced risk of colon cancer, and the evidence is consistent. The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR 2007) concluded that the evidence for a protective effect of physical activity against colon cancer was convincing [27]; the International Agency for Research on Cancer (IARC) judged the evidence to be ‘sufficient’ for life-long high-level physical activity [28]. A meta-analysis of 21 studies reported a 27% decreased risk of proximal colon cancer and an almost identical 26% decreased risk of distal colon cancer among the most physically active compared with the least active individuals [29]. In contrast, physical activity appears to be unrelated to rectal cancer [30].

Cohort studies have shown that the inverse association between physical activity and risk of colon cancer is independent of body mass index (BMI) [31–34]. Exercise need be neither intense nor of long duration for benefits to be seen [35].

2.1.2. Endometrial cancer

A meta-analysis of five prospective studies examining occupational activity and endometrial cancer suggested a 20% reduction in risk of this cancer for people in the highest versus the lowest category of physical activity [36], with some evidence that the effect may be stronger in obese women. A meta-analysis of prospective studies examining recreational activity indicated a similar level of protection [37], most studies being adjusted for BMI. Voskuil et al. [38] drew the same conclusion from a systematic review of evidence from 20 cohort or case–control studies, which indicated a protective effect of physical activity independent of body weight. Findings from studies which focused on a particular type of exercise (walking for example) are less consistent, and this is also true for studies of vigorous activity.

2.1.3. Breast cancer

Much of the evidence linking physical activity with cancer of the breast comes from studies of post-menopausal breast cancer, for which the evidence is judged 'probable' by the WCRF/AICR [39]; the IARC drew a similar conclusion [28]. The evidence for pre-menopausal breast cancer is less certain. Results from the Netherlands cohort study [40] suggested an inverse association with recreational physical activity (not restricted to sports activities, but including gardening for example); total physical activity of more than 90 min per day, compared with less than 30 min per day, was associated with a risk reduction of about 25%. The relationship between physical activity and breast cancer risk shows a dependency on exercise intensity and duration [41] and is observed across a wide range of BMIs [42].

2.2. Other cancers for which evidence is more limited or less consistent

2.2.1. Lung cancer

The evidence considered for the WCRF/AICR 2007 report was only 'suggestive' of a beneficial effect of physical activity for lung cancer risk [27]. Particular note was taken of the likelihood of reverse causation due to chronic lung disease. Some case–control and cohort studies do show a lower risk of lung cancer with increased physical activity, but the evidence is not consistent and a mechanistic explanation is lacking. Others have reviewed the evidence more recently and drawn similar conclusions [26]. Leitzmann et al. [43] conducted a prospective study in a cohort derived from the large NIH-AARP Diet and Health Study and showed that high versus low physical activity was associated with a 22% decreased risk of lung cancer among ex-smokers and a 23% decreased risk among current smokers, but was unrelated to lung cancer among never smokers, suggestive of residual confounding by cigarette smoking.

2.2.2. Ovarian cancer

Evidence for a link between physical activity and risk of ovarian cancer is very limited. Some evidence is available from individual studies and meta-analyses but is inconsistent. A recent report from the NIH-AARP Diet and Health Study found no association between either physical activity or sedentary behavior at baseline (adjusted for body fatness) and ovarian cancer risk over a 10-year follow-up [44]. This is in contrast with findings from an early meta-analysis of 13 cohort and case–control studies that suggested a weak protective effect of recreational physical activity [45], and from the Iowa Women's Health Study, which suggested an increased risk, especially for vigorous physical activity [46]. Other case–control and cohort studies have reported a beneficial effect of recreational and habitual physical activity, but limitations in study design generally compromise the conclusions drawn [47–49].

2.2.3. Pancreatic cancer

Although there is a reasonable volume of literature examining physical activity and risk of pancreatic cancer, the evidence is inconsistent. One pooled analysis reported a marginally significant protective effect of total physical activity and recreational physical activity [50]. In contrast, results of meta-analyses of high versus low categories are not consistent in their findings [51,52]. Inconsistency is also seen for different types of physical activity (such as recreational or occupational activity), and overall there is no evidence for an effect of physical activity on risk of pancreatic cancer.

2.2.4. Prostate cancer

A meta-analysis of 19 cohort studies and 24 case–control studies found a 10% reduced risk of prostate cancer when comparing high versus low levels of physical activity [53]. Apparent benefit was observed for both recreational and occupational types of physical activity. Investigations of activity intensity have yielded stronger relations with vigorous activity. The apparent protective effect of physical activity on risk for prostate cancer does not appear to vary across subgroups of men.

2.2.5. Renal cancer

Evidence linking physical activity with renal cancers is accumulating, with a recent meta-analysis of 19 studies showing an inverse relationship between physical activity and risk of renal cancer [54]. Individuals with high versus low physical activity levels showed a 22% decreased risk of renal cancer; this association was not modified by adiposity or other potential effect-modifying variables.

2.2.6. Gastric cancer

A recent meta-analysis of seven cohort studies and nine case–control studies reported a 21% decreased risk of gastric cancer for individuals with high versus low levels of physical activity [55]. Risk reduction was apparent for cancers of the cardia (the first portion of the stomach closest to the esophagus) and non-cardia cancers, and findings were consistent across categories of gender, study design, and study geographic location.

2.3. Sedentary behavior and cancer

Numerous epidemiologic studies have suggested a direct positive relationship between sedentary behavior and risk of cancers at various sites, independently of BMI or physical activity [56]. For example, Howard et al. [57] found a 61% increased risk of total colon cancer in men with ≥9 h per day spent watching television or video in a prospective study from the NIH-AARP Diet and Health cohort. A high versus low level of recreational sitting time (≥6 h versus <3 h per day) was associated with a 55% increased ovarian cancer risk in the Cancer Society Cancer Prevention Study II Nutrition Cohort [58], and this relationship was not modified by levels of physical activity. One study showed that a lifestyle which includes sitting for long periods of the day may increase the risk of endometrial cancer by 45% [37]. Similarly, in their study among Chinese women, Pronk and colleagues showed a statistically non-significant 23% increase in breast cancer risk associated with high versus low lifelong occupational sitting time [59]. Also, prolonged television/video time was associated with a 28% increased risk of total prostate cancer among obese men, although that finding was not statistically significant [60].

2.4. Biological mechanisms relating physical activity to cancer

Although there are numerous plausible mechanisms linking physical activity with risk of cancer at various sites, most of those that have been proposed are also linked with overweight and obesity. With current available evidence it is difficult to disentangle the effects of physical activity from effects on body weight, although independent physical activity effects have been described [61] (Fig. 6). Due to cancer site specificity of carcinogenesis it is likely that mechanisms explaining associations between physical activity and risk of cancer may also show some site specificity.

Increased body fatness is associated with increased concentrations of circulating estrogens and androgens in women, an increased production of pro-inflammatory cytokines, and a lower concentration of sex-hormone-binding globulin (SHBG). Insulin

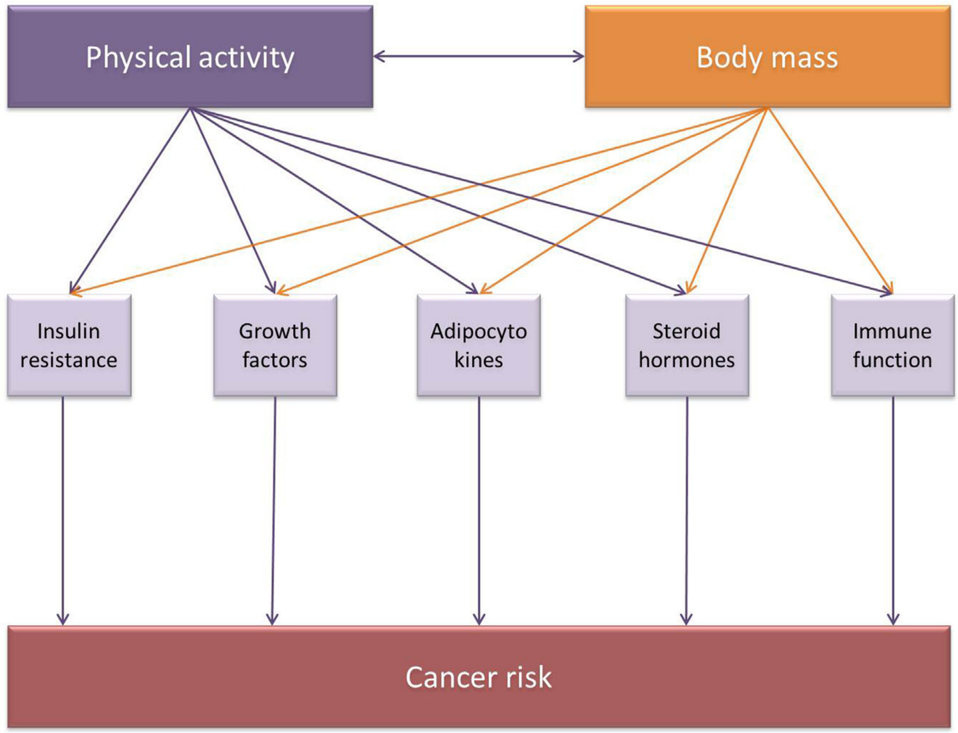

Fig. 6. Hypothesized mechanisms linking physical activity to cancer. These include insulin resistance, growth factors, adipocytokines, steroid hormones, and immune function. Physical activity may affect these pathways directly or indirectly by reducing body mass.

resistance is also characteristic of high adiposity. These factors have been associated with an increased risk of cancer at various sites. Higher concentrations of circulating estrogens and androgens are linked with an increased risk of pre- and post-menopausal breast cancer [62] and endometrial cancer, whilst increased concentrations of markers of inflammation are associated with an increased risk of cancer at many sites [63]. Additionally, insulin resistance may be linked to increased risk of several cancers, including those of the breast, colon and endometrium.

Physical activity can reduce body fatness and may influence cancer risk indirectly through associated beneficial effects on sex hormones and inflammatory cytokines and with a decrease in insulin resistance. However, effects of physical activity on growth factor concentrations and their binding proteins are not clear; studies report effects in different directions [64].

There may be beneficial effects of physical activity independent of effects on body fatness, but this is not yet well understood. Certainly there is evidence that physical activity can mitigate effects on inflammatory markers of being overweight [65]. Physical activity may also reduce hyperinsulinemia independently of changes in body adiposity [66,67].

Other plausible mechanisms by which physical activity might reduce cancer risk include effects on immune function and on oxidative stress and associated damage to DNA. The relationship between physical activity and immune function is complex; there is some evidence for a J-shaped curve between intensity of exercise and measures of immune function, but findings are inconsistent and it is difficult to draw conclusions. Oxidative damage to DNA can lead to mutations and cancer. Physical activity, especially vigorous activity, can increase the production of reactive oxygen species and increase the risk of DNA damage, but may also upregulate DNA repair mechanisms [68,69]. The overall effect of physical activity will depend on the balance between these two processes.

Increased gut motility may influence colon cancer risk by lowering the exposure of colon mucosa to food carcinogens [70].

2.5. Biological mechanisms relating sedentary behavior to cancer

Several biologic mechanisms may mediate the adverse association between sedentary behavior and cancer. Most available evidence supports a role of decreased energy expenditure accompanied by increased weight gain over time, leading to cancer development. Adiposity may facilitate carcinogenesis through a number of pathways, as discussed above, including elevations of estrogens in post-menopausal women, insulin resistance, perturbations in the insulin-like growth factor axis, and low-grade systemic inflammation [71]. The WCRF panel concluded that the evidence that sedentary living causes weight gain, overweight, and obesity is convincing [27]. According to a study conducted in the adult population of the European Union, those who spent more than 35 h per week sitting during their leisure time were approximately 60% more likely to be obese than those who spent less than 15 h per week sitting during their leisure time [72]. Also, there is evidence that the biological mechanisms through which sedentary habits operate are independent from those related to physical activity. For example, even in physically active adults, significant positive relations of TV time to metabolic risk and mortality have been observed [14,73]. Therefore, large amounts of sedentary time (notably television viewing) are highly likely to contribute indirectly to cancer risk through decreased energy expenditure and an increased risk of weight gain.

3. Justification for recommendation

3.1. Importance of a physically active lifestyle for cancer prevention

According to recent estimates from the Lancet Physical Activity Series Working Group, inadequate physical activity levels cause 9% of breast cancer cases in Europe. Data vary by country, showing that 4% of breast cancer cases in Greece and 19% of breast cancer cases in Malta and Serbia could be prevented by adequate levels of physical activity. Similarly, inadequate physical activity levels cause 10% of colon cancer cases in Europe, ranging from 4.6% of colon cancer cases in Greece to 21% of colon cancer cases in Malta [74].

3.2. Global public health action and individual responsibility for increasing physical activity

Most available research suggests that global public health action is needed to increase an individual's physical activity levels. Target organizations or initiatives include schools, businesses, policy, advocacy, nutrition, recreation, planning, transport agencies, and health-care organizations. Notwithstanding the significance of the built environment, individual responsibility for achieving and maintaining adequate levels of physical activity is important given the available evidence linking increased physical activity to decreased cancer risk. Setting quantitative targets represents an important individual strategy to increase physical activity levels. However, along with goal-setting, there are additional factors that play a significant role, such as social support, behavioral reinforcement through self-reward, and relapse prevention.

3.3. Physical activity in different phases of life

Little is known about whether the potential for cancer prevention associated with increased physical activity is dependent on the timing of physical activity. Data from a recent meta-analysis show breast cancer risk reductions of 17% for physical activity carried out at age $\geq$50 years, 11% for physical activity performed at ages 25–50 years, and 10% for physical activity carried out age $<$25 years [75]. This suggests that physical activity performed at any age is associated with decreased breast cancer risk, but risk reduction may be slightly more pronounced when physical activity is carried out during late adulthood than when it is performed during early adulthood or mid-adulthood. Certain phases of hormonal change may have characteristic biological consequences that differentially affect the relation between physical activity and cancer.

3.4. Physical activity in cancer survivors

Randomized controlled trials show a beneficial effect of physical activity on body composition, physical fitness, quality of life, anxiety, and self-esteem in cancer survivors [76]. Observational studies that have addressed the association between physical activity and risk of death among survivors of cancer suggest that physical activity prolongs overall and cancer-specific survival [77]. For example, a recent meta-analysis of prospective cohort studies concluded that physical activity before or after diagnosis reduces mortality from colorectal cancer [78]. Also, there is evidence suggestive of a beneficial effect of physical activity after breast cancer diagnosis on all-cause mortality [79]. For recreational activity a dose response is evident [80]. There is also evidence for a protective effect of physical activity after breast cancer diagnosis on breast cancer mortality [81]. Pre-diagnosis physical activity was associated with reduced risk of mortality from all causes among women with endometrial cancer, but that relationship was no longer evident after adjustment for BMI [82]. This suggests that adiposity explains the apparent protective effect of physical activity on endometrial cancer survival. Taken together, observational studies of cancer survivors show that physical activity is independently associated with decreased risk of all-cause [77], breast-cancer-specific and colon-cancer-specific mortality [83], but there is insufficient evidence for a beneficial effect of physical activity on mortality for survivors of other cancers. Existing randomized trials have been characterized by small sample sizes, short follow-up periods, and lack of standardization of physical activity interventions across studies, precluding definitive conclusions in terms of a causal relation between increased physical activity and prolonged cancer survival [84]. The sparse observational data available show that time spent sedentary is associated with increased risk of mortality among colorectal cancer survivors [85] but not among breast cancer survivors [86].

4. Conclusion

Substantial observational epidemiologic evidence suggests that physical activity is related to decreased risks of colon, endometrial, and breast cancers, whereas the data for an apparent protective effect of physical activity is weaker for cancers of the lung, pancreas, ovary, prostate, kidney, and stomach. Although the etiologic mechanisms through which physical activity may reduce cancer risk remain inadequately understood, possible biologic pathways include insulin resistance, growth factors, adipokines, steroid hormones, and immune function. Recent epidemiologic investigations have also supported the hypothesis that sedentary behavior represents an independent risk factor for cancer, although additional data are needed. In cancer survivors, physical activity appears to impart beneficial effects on body composition, physical fitness, quality of life, anxiety, and self-esteem. In addition, physical activity has been proposed to prolong cancer survival, but a causal link remains to be established. Taken together, the fourth edition of the European Code against Cancer (Box 1) advocates action-oriented recommendations for the general public. The European Code against Cancer Working Group has agreed on the following recommendation:

Box 1. European Code Against Cancer.

EUROPEAN CODE AGAINST CANCER

12 ways to reduce your cancer risk

1. Do not smoke. Do not use any form of tobacco
2. Make your home smoke free. Support smoke-free policies in your workplace
3. Take action to be a healthy body weight
4. Be physically active in everyday life. Limit the time you spend sitting
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks
   - Avoid processed meat; limit red meat and foods high in salt
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions
9. Find out if you are exposed to radiation from naturally high radon levels in your home; take action to reduce high radon levels
10. For women:
    - Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby
    - Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT
11. Ensure your children take part in vaccination programmes for:
    - Hepatitis B (for newborns)
    - Human papillomavirus (HPV) (for girls)
12. Take part in organised cancer screening programmes for:
    - Bowel cancer (men and women)
    - Breast cancer (women)
    - Cervical cancer (women)

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.

"Be physically active in everyday life. Limit the time you spend sitting."

Conflict of interest

The authors declare no conflict of interest.

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